Transcriptomic profiling of non-neoplastic ductal salivary gland epithelial cell lines of patients with primary Sjogren's syndrome

Menelaos N. Manoussakis

Department of Pathophysiology

School of Medicine, NKUA

# Primary Sjogren's syndrome – Autoimmune epitheliitis

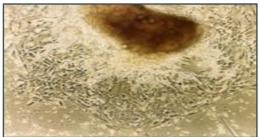
- Chronic exocrinopathy systemic disease
  - dysfunction destruction of salivary and lachrymal glands
  - chronic T & B lymphocyte infiltrations
  - intense autoantibody responses
  - Chronic immune activation: development of B-cell lymphoma
  - Major role of ductal salivary epithelia in pathogenesis

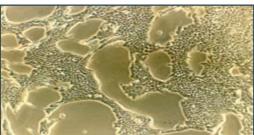
### Ex vivo study of epithelial cells

#### ESTABLISHMENT OF SALIVARY GLAND EPITHELIAL CELL CULTURES

- long-term cultured cell lines
- non-neoplastic
- from one MSG lobule
- obtained during diagnostic biopsy (informed consent)





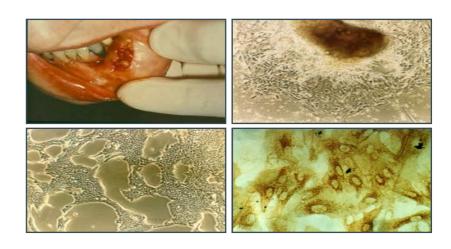


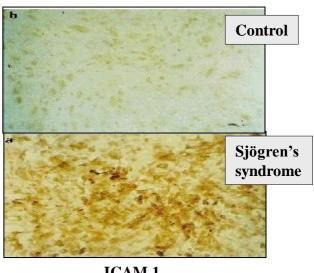


- Phenotypic characteristics (ductal type)
- Functional properties
  - immunologic function
    - interaction with immune cells
    - non-specific immunity
  - response to pro-apoptotic signals
  - response to hormones
  - cell type-specific functions
- Specific research
  - genetic make-up
  - epigenetic influences
  - infections
  - therapeutic interventions

## **Cultured SS-SGEC lines:** INDICATE THE CELL-INTRINSIC ACTIVATION PHENOTYPE

- closely correlates with the histologic and systemic features of the disease
- increased constitutive expression of various molecules (vs controls)
  - analogous changes are also evidenced in-situ in the ductal epithelial tissues of SS patients
- various cell-autonomous functional aberrations
  - constitutive activation of NF-κB signaling pathway
  - deficient response to estrogens
  - increased sensitivity to apoptosis





ICAM.1

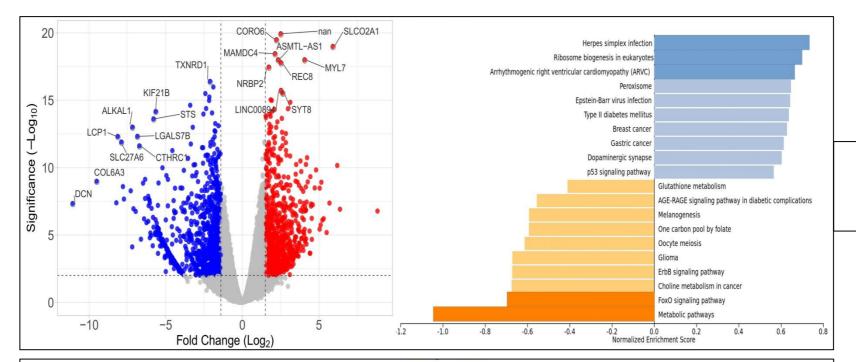
# Transcriptomic profiling: SGEC groups studied

SGEC GROUPS	Number of SGEC lines studied	From patients who fulfilled SS Classification Criteria	From patients who presented features of severe SS *
CONTROLS	15	NO	NA
SS-INTERMEDIATE	8	YES	NO
SS-SEVERE	9	YES	YES

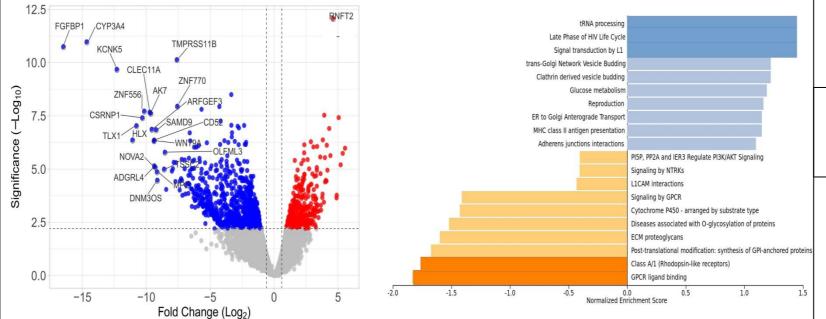
NA: not applicable.

<sup>\*</sup>Features of severe disease: severe extra-glandular manifestations and display clinical or serological manifestations that constitute prognostic markers for the development of B-cell lymphoma in SS.

### **RESULTS-1**



INTERMEDIATE VS. CONTROLS



SEVERE VS. CONTROLS

#### **RESULTS-2**

